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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SAJJADI, FEREYDOUN GHOTB	
ART UNIT	**PAPER NUMBER**
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,250	NEMEROW ET AL.	
	Examiner	Art Unit	
	Fereydoun G. Sajjadi	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR.1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 June 2006*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,10-54 and 57-79* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-7,10-54 and 57-79* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-7, 10-54 and 57-79 are pending in the application.

Election/Restrictions

Restriction is required under 35 U.S.C. 121 and 372.

1. This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-30, 35 and 40-45, drawn to a modified adenovirus fiber, comprising a modification to the fiber protein shaft, whereby binding of the fiber or of a viral particle containing such fiber to the Coxsackie-Adenovirus Receptor (CAR) is reduced or eliminated compared to the unmodified fiber.

Group II, claim(s) 1, 31 and 33, drawn to a modified adenovirus fiber, comprising a modification to the fiber protein shaft and an additional modification in the fiber protein, whereby the modified fiber binds to a receptor other than CAR.

Group III, claim(s) 1, 32, 34 and 36-39 drawn to a modified adenovirus fiber, comprising a modification to the fiber protein shaft and an additional modification in the fiber knob protein, whereby the binding of the modified fiber to CAR is further reduced or eliminated.

Group IV, claim(s) 46-54 and 57, drawn to a nucleic acid molecule that encodes a modified protein shaft adenovirus fiber, a vector comprising the same, and a cell comprising said nucleic acid.

Group V, claim(s) 58, 60-65 and 72, drawn to an adenovirus particle comprising a modified shaft fiber protein.

Group VI, claim(s) 58-59, drawn to an adenovirus particle comprising a modified shaft fiber protein and a modified penton protein.

Group VII, claim(s) 58 and 66-68, drawn to an adenovirus particle comprising a modified shaft fiber protein and a modification to the capsid whereby binding of the viral particle to HSP or integrin is altered.

Group VIII, claim(s) 58 and 69-71, drawn to an adenovirus particle comprising a modified shaft fiber protein and a modification in the fiber knob to further reduce CAR binding.

Group IX, claim(s) 73-74 and 76, drawn to a method of detargeting an adenoviral vector, comprising producing an adenviral particle comprising one modification to the fiber protein shaft.

Group X, claim(s) 73, 75 and 77, drawn to a method of detargeting an adenoviral vector, comprising producing an adenviral particle comprising at least two modifications to the fiber protein.

Group XI, claim(s) 78-79, drawn to a method comprising introducing an adenoviral particle comprising a modification to the fiber protein shaft into cells, and introducing the cells into a subject.

2. Group I-XI claims encompass a plurality of distinct inventions exemplified by structurally distinct modifications of the regions of the adenovirus shaft protein that comprise distinct nucleic acid and polypeptide sequences. These are exemplified by SEQ ID NOS: 58, 66, 67 and 68 corresponding to the Ad37, Ad 8, Ad9 and Ad15 third repeats respectively ; SEQ ID NOS: 46, and 47, corresponding to the Ad2 and Ad5 twenty first repeat; SEQ ID NOS: 48, 49, 59, 60 and 61, corresponding to the consensus, Ad 37 Ad8, Ad 9 and Ad61 last repeats respectively. Because the polypeptide and nucleic acids have distinct structural sequences, not commonly shared, they lack unity of invention. Applicant is required to choose a single, specific

SEQ ID NO for each of the modified regions of the shaft or capsid proteins, commensurate with the Ad species elected, should any of the inventions of Groups I-XI be elected for examination. While nucleic acids and their correspondingly encoded polypeptides are also structurally distinct, under the rules for unity of invention, they are examined together. However, said rule does not apply to distinct chimeric sequences encoding distinct polypeptides. Hence the claims encompass an improper Markush Grouping, lacking unity of invention (In *re* *>*Harnisch*<, 631 F.2d 716, 206 USPQ 300 (CCPA 1980). This is not a species restriction requirement.

The inventions listed as Groups I-XI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

37 CFR 1.475 (e) states:

"The determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim."

In view of 37 CFR 1.475 (e), Groups I-III are considered a plurality of the inventions listed in claim 1; and Groups V-VIII are considered a plurality of the inventions listed in claim 58; and Groups IX-X are considered a plurality of the inventions listed in claim 73.

The inventions listed as Groups I-XI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features. According to PCT Rule 13.2, unity of invention exists only when a shared same or corresponding special technical feature is a contribution over the prior art. The technical feature, which is shared by Groups I-XI, is a modified adenovirus fiber protein shaft that in an adenoviral particle reduces binding to the CAR receptor. Groups I-XI do not share a special technical feature over the art because Vigne et al. (U.S. Patent No: 6,911,199; priority to Aug. 27, 1998), discloses targeted adenovirus vectors for delivery of heterologous genes, wherein modifications of the internal sites of the adenovirus fiber protein target the modified adenoparticles to specific cell types (Title and Abstract). Specifically disclosing that the fiber

protein can be modified to have a fiber shaft that is shorter than a wild-type fiber shaft, in particular by an in-frame deletion or by replacing it with the shaft from another serotype. The fiber shaft can be from subgroup C and comprises an in-frame deletion encompassing repeats 4 to 16 or repeats 4 to 19 or from subgroup C and has been shortened by replacing it with the shaft from serotype 3 (Ad3)...the fiber protein can be modified to be shorter than in the wild-type sequence. For example, the fiber protein can be modified to contain only repeats 1 to 3 and 17 to 22 of Ad5; repeats 1 to 3 and 20 to 22 of Ad5; or an adenovirus serotype 3 (Ad3) shaft in place of the endogenous Ad5 shaft (column 6). The method for targeting a specific cell type in accordance with the invention can be further enhanced by shortening the fiber protein shaft, e.g., such that the fiber shaft only contains repeats 1 to 3 and 17 to 22 of Ad5; repeats 1 to 3 and 20 to 22 of Ad5; or with an Ad3 shaft (column 7).

The claims in Groups I-XI are drawn to distinct products and methods that utilize distinct steps, requiring non-coextensive search and examination. Thus, it follows from the preceding analysis that the claimed inventions listed as Groups I-XI do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding technical features for the reasons set forth above.

Group I-XI claims are drawn to a product and the processes of making and using said product. The product and method are distinct, because the processes may be made applied to different adenoviruses having different mutations in their capsid proteins, thus, requiring non-coextensive search and examination. Thus, it follows from the preceding analysis that the claimed inventions listed as Groups I-XI do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding technical features for the reasons set forth above.

If an examiner (1) determines that the claims lack unity of invention and (2) requires election of a single invention, when all of the claims drawn to the elected invention are allowable (i.e., meet the requirements of 35 U.S.C. 101, 102, 103 and 112), the nonelected invention(s) should be considered for rejoinder. Any nonelected product claim that requires all the limitations of an allowable product claim, and any nonelected process claim that requires all the limitations of an allowable process claim, should be rejoined. See MPEP § 821.04 and § 821.04(a). Any nonelected processes of making

and/or using an allowable product should be considered for rejoinder following the practice set forth in MPEP § 821.04(b).

3. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

A specifically named single species of serotype C Ad2 or Ad5 adenovirus, as recited in claims 7, 15, 26, 43 and 62; a specifically named single species of serotype D Ad8, Ad9, Ad15, Ad19p or Ad37 modified fiber as recited in claims 11, 18, 28 and 30; a specifically named single species of Ad3 modified fiber knob mutations (Ad41 short fiber knob or Ad35 fiber knob; AB loop or CD loop; KO1 or KO12; AB loop or CD loop) as recited in claims 37-39 and 70-71. A specific type of adenoviral vector (gutless or replication conditional or oncolytic), as recited in claims 52 and 53. A specific single species of N-terminal modified fiber comprising at least 15, 16 or 17 amino acids, as recited in claim 61.

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

The claims are deemed to correspond to the species listed above in the following manner:

Claims 11, 18, 28, 30, 37-39, 52, 53, 61 and 70-71, and claims dependent therefrom correspond to all the species listed above.

The following claim(s) are generic: 1-7, 10-54 and 57-79.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: As the technical features (adenovirus serotypes, modifications in the shaft, fiber knob and capsid proteins) linking the members do not constitute a special technical feature as defined by PCT Rule 13.2, particularly since each of the species does not share a substantially common structural feature or function, the requirement for unity of invention is not fulfilled.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their divergent subject matter, restriction for examination purposes as indicated is proper. Thus, it would be unduly burdensome for the examiner to search all the claimed inventions being sought in the pending claims.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fereydoun G. Sajjadi whose telephone number is (571) 272-3311. The examiner can normally be reached on 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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